

1

# SEQUENCE LISTING

<110> Isaacs, John T.  
Denmeade, Samuel R.  
Lilja, Hans

<120> ACTIVATION OF PEPTIDE PRODRUGS BY hK2

<130> 07265-191001

<140> US 09/627,600

<141> 2000-07-28

<150> US 60/146,316

<151> 1999-07-29

<160> 135

<170> FastSEQ for Windows Version.4.0

<210> 1

<211> 11

<212> PRT

<213> Homo sapiens

<400> 1

His Lys Gly Gly Lys Ala His Arg Gly Thr Gln  
1 5 10

<210> 2

<211> 11

<212> PRT

<213> Homo sapiens

<400> 2

Ser Ser Ser Tyr Glu Glu Arg Arg Leu His Tyr  
1 5 10

<210> 3

<211> 11

<212> PRT

<213> Homo sapiens

<400> 3

Ser Ser Ser Tyr Glu Glu Arg Arg Leu His Tyr  
1 5 10

<210> 4

<211> 11

<212> PRT

<213> Homo sapiens

<400> 4

Val Gln Lys Asp Val Ser Gln Arg Ser Ile Tyr  
1 5 10

2

<210> 5  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 5  
 Asp Lys Ser Lys Gly His Phe His Met Ile Val  
 1 5 10

<210> 6  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 6  
 Gln Cys Ser Asn Thr Glu Lys Arg Leu Trp Val  
 1 5 10

<210> 7  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 7  
 Leu His Pro Ala His Gln Asp Arg Leu Gln His  
 1 5 10

<210> 8  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 8  
 Lys Ile Ser Tyr Pro Ser Ser Arg Thr Glu Glu  
 1 5 10

<210> 9  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 9  
 Gly Lys Ser Gln Asn Gln Val Arg Ile Pro Ser  
 1 5 10

<210> 10  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 10  
 Ser Ser Ser Tyr Glu Glu Arg Arg Leu Asn Tyr  
 1 5 10

<210> 11  
 <211> 11  
 <212> PRT

3

<213> Homo sapiens

<400> 11

Leu Ser His Glu Gln Lys Gly Arg Tyr Lys Gln  
1 5 10

<210> 12

<211> 3

<212> PRT

<213> Homo sapiens

<400> 12

Lys Arg Arg  
1

<210> 13

<211> 3

<212> PRT

<213> Homo sapiens

<400> 13

Ser Arg Arg  
1

<210> 14

<211> 3

<212> PRT

<213> Homo sapiens

<400> 14

Ala Arg Arg  
1

<210> 15

<211> 3

<212> PRT

<213> Homo sapiens

<400> 15

His Arg Arg  
1

<210> 16

<211> 3

<212> PRT

<213> Homo sapiens

<400> 16

Gln Arg Arg  
1

<210> 17

<211> 3

<212> PRT

<213> Homo sapiens

<400> 17

4

Ala Phe Arg

1

<210> 18

<211> 3

<212> PRT

<213> Homo sapiens

<400> 18

Ala Gln Arg

1

<210> 18

<211> 3

<212> PRT

<213> Homo sapiens

<400> 18

Ala Lys Arg

1

<210> 20

<211> 3

<212> PRT

<213> Homo sapiens

<400> 20

Ala Arg Lys

1

<210> 21

<211> 3

<212> PRT

<213> Homo sapiens

<400> 21

Ala His Arg

1

<210> 22

<211> 4

<212> PRT

<213> Homo sapiens

<400> 22

Gln Lys Arg Arg

1

<210> 23

<211> 4

<212> PRT

<213> Homo sapiens

<400> 23

Lys Ser Arg Arg

1

5

<210> 24  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 24  
Ala Lys Arg Arg  
1

<210> 25  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 25  
Lys Lys Arg Arg  
1

<210> 26  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 26  
His Lys Arg Arg  
1

<210> 27  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 27  
Lys Ala Phe Arg  
1

<210> 28  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 28  
Lys Ala Gln Arg  
1

<210> 29  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 29  
Lys Ala Lys Arg  
1

<210> 30  
<211> 4  
<212> PRT

9

<213> Homo sapiens

<400> 30  
Lys Ala Arg Lys  
1

<210> 31  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 31  
Lys Ala His Arg  
1

<210> 32  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 32  
Lys Arg Arg Leu  
1

<210> 33  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 33  
Ser Arg Arg Leu  
1

<210> 34  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 34  
Ala Arg Arg Leu  
1

<210> 35  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 35  
Ala Arg Arg Ser  
1

<210> 36  
<211> 4  
<212> PRT  
<213> Homo sapiens

<400> 36

7

His Arg Arg Ala

1

<210> 37

<211> 4

<212> PRT

<213> Homo sapiens

<400> 37

Gln Arg Arg Leu

1

<210> 38

<211> 4

<212> PRT

<213> Homo sapiens

<400> 38

Ala Phe Arg Leu

1

<210> 39

<211> 4

<212> PRT

<213> Homo sapiens

<400> 39

Ala Gln Arg Leu

1

<210> 40

<211> 4

<212> PRT

<213> Homo sapiens

<400> 40

Ala Lys Arg Leu

1

<210> 41

<211> 4

<212> PRT

<213> Homo sapiens

<400> 41

Ala Arg Lys Leu

1

<210> 42

<211> 4

<212> PRT

<213> Homo sapiens

<400> 42

Ala His Arg Leu

1

<210> 43  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 43  
 His Ala Gln Lys Arg Arg Leu  
 1 5

<210> 44  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 44  
 Gly Gly Lys Ser Arg Arg Leu  
 1 5

<210> 45  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 45  
 His Glu Gln Lys Arg Arg Leu  
 1 5

<210> 46  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 46  
 His Glu Ala Lys Arg Arg Leu  
 1 5

<210> 47  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 47  
 Gly Gly Gln Lys Arg Arg Leu  
 1 5

<210> 48  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 48  
 His Glu Gln Lys Arg Arg Ala  
 1 5

<210> 49  
 <211> 7  
 <212> PRT



<213> Homo sapiens

<400> 49

Gly Gly Ala Lys Arg Arg Leu  
1 5

<210> 50

<211> 7

<212> PRT

<213> Homo sapiens

<400> 50

His Glu Gln Lys Arg Arg Ser  
1 5

<210> 51

<211> 7

<212> PRT

<213> Homo sapiens

<400> 51

Gly Gly Lys Lys Arg Arg Leu  
1 5

<210> 52

<211> 7

<212> PRT

<213> Homo sapiens

<400> 52

Gly Gly His Lys Arg Arg Leu  
1 5

<210> 53

<211> 5

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> 1

<223> Xaa = Boc (t-butoxy carbonyl)

<221> VARIANT

<222> 5

<223> Xaa = AMC (aminomethylcoumarin)

<400> 53

Xaa Phe Ser Arg Xaa  
1 5

<210> 54

<211> 5

<212> PRT

<213> Homo sapiens

<220>

10

<221> VARIANT  
 <222> 1  
 <223> Xaa = Boc (t-butoxy carbonyl)

<221> VARIANT  
 <222> 5  
 <223> Xaa = AMC (aminomethylcoumarin)

<400> 54  
 Xaa Gln Gly Arg Xaa  
 1 5

<210> 55  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> VARIANT  
 <222> 1  
 <223> Xaa = H (hydrogen)

<221> VARIANT  
 <222> 5  
 <223> Xaa = AMC (aminomethylcoumarin)

<400> 55  
 Xaa Pro Phe Arg Xaa  
 1 5

<210> 56  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> VARIANT  
 <222> 1  
 <223> Xaa = Boc (t-butoxy carbonyl)

<221> VARIANT  
 <222> 5  
 <223> Xaa = AMC (aminomethylcoumarin)

<400> 56  
 Xaa Val Pro Arg Xaa  
 1 5

<210> 57  
 <211> 5  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> VARIANT  
 <222> 1  
 <223> Xaa = H-D (free amine without protecting group)

<221> VARIANT  
<222> 5  
<223> Xaa = AMC (aminomethylcoumarin)

<400> 57  
Xaa Val Leu Lys Xaa  
1 5

<210> 58  
<211> 5  
<212> PRT  
<213> Homo sapiens

<220>  
<221> VARIANT  
<222> 1  
<223> Xaa = Tos (4-Toluenesulphonyl)

<221> VARIANT  
<222> 5  
<223> Xaa = AMC (aminomethylcoumarin)

<400> 58  
Xaa Gly Pro Arg Xaa  
1 5

<210> 59  
<211> 5  
<212> PRT  
<213> Homo sapiens

<220>  
<221> VARIANT  
<222> 1  
<223> Xaa = Tos (4-Toluenesulphonyl)

<221> VARIANT  
<222> 5  
<223> Xaa = AMC (aminomethylcoumarin)

<400> 59  
Xaa Gly Pro Lys Xaa  
1 5

<210> 60  
<211> 5  
<212> PRT  
<213> Homo sapiens

<220>  
<221> VARIANT  
<222> 1  
<223> Xaa = Z (carbobenzyloxy)

<221> VARIANT  
<222> 5

12

<223> Xaa = AMC (aminomethylcoumarin)

<400> 60

Xaa Leu Leu Arg Xaa  
1 5

<210> 61

<211> 5

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> 1

<223> Xaa = 2 (carbobenzyloxy)

<221> VARIANT

<222> 5

<223> Xaa = AMC (aminomethylcoumarin)

<400> 61

Xaa Val Val Arg Xaa  
1 5

<210> 62

<211> 5

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> 1

<223> Xaa = 2 (carbobenzyloxy)

<221> VARIANT

<222> 5

<223> Xaa = AMC (aminomethylcoumarin)

<400> 62

Xaa Ala Arg Arg Xaa  
1 5

<210> 63

<211> 6

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> 1

<223> Xaa = H (hydrogen)

<221> VARIANT

<222> 5

<223> Xaa = AMC (aminomethylcoumarin)

<400> 63

13

Xaa Arg Gln Arg Arg Xaa  
1 5

<210> 64  
<211> 10  
<212> PRT  
<213> Homo sapiens

<220>  
<221> VARIANT  
<222> 1  
<223> Xaa = Mu (morphocurea)

<221> VARIANT  
<222> 10  
<223> Xaa = AMC (aminomethylcoumarin)

<400> 64  
Xaa Ala Pro Val Leu Ile Leu Ser Arg Xaa  
1 5 10

<210> 65  
<211> 9  
<212> PRT  
<213> Homo sapiens

<220>  
<221> VARIANT  
<222> 1  
<223> Xaa = Mu (morphocurea)

<221> VARIANT  
<222> 9  
<223> Xaa = AMC (aminomethylcoumarin)

<400> 65  
Xaa Val Pro Leu Ile Gln Ser Arg Xaa  
1 5

<210> 66  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 66  
Gly His Glu Gln Lys Arg Arg Leu  
1 5

<210> 67  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 67  
Gly Gly Gly Lys Ala Arg Arg Leu  
1 5

<210> 68  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 68  
Gly Gly Gly Lys Ala His Arg Leu  
1 5

<210> 69  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 69  
Gly Pro Ala His Gln Arg Arg Leu  
1 5

<210> 70  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 70  
Gly Ser Lys Gly His Phe Arg Leu  
1 5

<210> 71  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 71  
Gly Ser Lys Gly His Arg Arg Leu  
1 5

<210> 72  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 72  
Gly Lys Asp Val Ser Arg Arg Leu  
1 5

<210> 73  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 73  
Gly Ser Gln Asn Gln Arg Arg Leu  
1 5

<210> 74  
<211> 8  
<212> PRT

15

<213> Homo sapiens

<400> 74

Gly Ser Tyr Pro Ser Arg Arg Leu  
1 5

<210> 75

<211> 8

<212> PRT

<213> Homo sapiens

<400> 75

Gly Ser Tyr Pro Ser Ser Arg Leu  
1 5

<210> 76

<211> 8

<212> PRT

<213> Homo sapiens

<400> 76

Gly His Glu Gln Lys Gly Arg Leu  
1 5

<210> 77

<211> 8

<212> PRT

<213> Homo sapiens

<400> 77

Gly Ser Asn Thr Glu Arg Arg Leu  
1 5

<210> 78

<211> 8

<212> PRT

<213> Homo sapiens

<400> 78

Gly Ser Tyr Glu Glu Arg Arg Leu  
1 5

<210> 79

<211> 8

<212> PRT

<213> Homo sapiens

<400> 79

Gly Lys Asp Val Ser Gly Arg Leu  
1 5

<210> 80

<211> 8

<212> PRT

<213> Homo sapiens

<400> 80

16

Gly Ser Asn Thr Glu Lys Arg Leu  
1 5

<210> 81  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 81  
Gly Ser Lys Gly His Phe His Leu  
1 5

<210> 82  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 82  
Gly Ser Gln Asn Gln Val Arg Leu  
1 5

<210> 83  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 83  
Gly Pro Leu Ile Leu Ser Arg Leu  
1 5

<210> 84  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 84  
Gly Ser Tyr Glu Glu Arg His Leu  
1 5

<210> 85  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 85  
Gly Lys Asp Val Ser Gly His Leu  
1 5

<210> 86  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 86  
Gly Gly Gly Lys Ala His His Leu  
1 5



17

<210> 87  
 <211> 8  
 <212> PRT  
 <213> Homo sapiens

<400> 87  
 Gly Ser Asn Thr Glu Lys His Leu  
 1 5

<210> 88  
 <211> 8  
 <212> PRT  
 <213> Homo sapiens

<400> 88  
 Gly Pro Ala His Gln Asp Arg Leu  
 1 5

<210> 89  
 <211> 8  
 <212> PRT  
 <213> Homo sapiens

<400> 89  
 Gly His Glu Gln Lys Gly His Leu  
 1 5

<210> 90  
 <211> 8  
 <212> PRT  
 <213> Homo sapiens

<400> 90  
 Gly Pro Ala His Gln Asp His Leu  
 1 5

<210> 91  
 <211> 8  
 <212> PRT  
 <213> Homo sapiens

<400> 91  
 Gly Ser Tyr Pro Ser Ser His Leu  
 1 5

<210> 92  
 <211> 8  
 <212> PRT  
 <213> Homo sapiens

<400> 92  
 Gly Ser Gln Asn Gln Val His Leu  
 1 5

<210> 93  
 <211> 8  
 <212> PRT

<213> Homo sapiens

<400> 93

Gly His Ala Gln Lys Arg Arg Leu  
1 5

<210> 94

<211> 7

<212> PRT

<213> Homo sapiens

<400> 94

Gly Gly Lys Ser Arg Arg Leu  
1 5

<210> 95

<211> 8

<212> PRT

<213> Homo sapiens

<400> 95

Gly His Glu Ala Lys Arg Arg Leu  
1 5

<210> 96

<211> 7

<212> PRT

<213> Homo sapiens

<400> 96

Gly Gly Gln Lys Arg Arg Leu  
1 5

<210> 97

<211> 8

<212> PRT

<213> Homo sapiens

<400> 97

Gly His Glu Gln Lys Arg Arg Ala  
1 5

<210> 98

<211> 7

<212> PRT

<213> Homo sapiens

<400> 98

Gly Gly Ala Lys Arg Arg Leu  
1 5

<210> 99

<211> 8

<212> PRT

<213> Homo sapiens

<400> 99

19

Gly His Glu Gln Lys Arg Arg Ser  
1 5

<210> 100  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 100  
Gly Gly Lys Lys Arg Arg Leu  
1 5

<210> 101  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 101  
Gly Gly His Lys Arg Arg Leu  
1 5

<210> 102  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 102  
Gly Gly Lys Ala Phe Arg Leu  
1 5

<210> 103  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 103  
Gly Ala Glu Gln Lys Arg Arg Leu  
1 5

<210> 104  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 104  
Gly Gly Lys Ala Gln Arg Leu  
1 5

<210> 105  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 105  
Gly Gly Lys Ala Arg Arg Leu  
1 5

20

<210> 106  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 106  
 Gly Gly Lys Gln Arg Arg Leu  
 1 5

<210> 107  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 107  
 Gly Gly Lys His Arg Arg Leu  
 1 5

<210> 108  
 <211> 8  
 <212> PRT  
 <213> Homo sapiens

<400> 108  
 Gly His Glu Gln Ala Arg Arg Leu  
 1 5

<210> 109  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 109  
 Gly Gly Lys Ala Lys Arg Leu  
 1 5

<210> 110  
 <211> 8  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> VARIANT  
 <222> 8  
 <223> Xaa = dL which is an isomer of Leu

<400> 110  
 Gly His Glu Gln Lys Arg Arg Xaa  
 1 5

<210> 111  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 111  
 Gly Gly Lys Ala Arg Arg Ser

21

1 5

<210> 112  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 112  
 Gly Gly Lys Ala Arg Lys Leu  
 1 5

<210> 113  
 <211> 8  
 <212> PRT  
 <213> Homo sapiens

<400> 113  
 Gly His Glu Gln Lys Arg Arg Glu  
 1 5

<210> 114  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 114  
 Gly Gly Lys Ala His Arg Leu  
 1 5

<210> 115  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 115  
 Gly Gly Lys Ala Asn Arg Leu  
 1 5

<210> 116  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 116  
 Gly Gly Lys Ala Arg Gln Leu  
 1 5

<210> 117  
 <211> 7  
 <212> PRT  
 <213> Homo sapiens

<400> 117  
 Gly Gly Lys Ala Arg His Leu  
 1 5

<210> 118

22

<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 118  
Gly Gly Lys Ala Arg Asn Leu  
1 5

<210> 119  
<211> 7  
<212> PRT  
<213> Homo sapiens

<220>  
<221> VARIANT  
<222> 5  
<223> Xaa = dR which is an isomer of Arg

<400> 119  
Gly Gly Lys Ala Xaa Arg Leu  
1 5

<210> 120  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 120  
Gly Gly Lys Ala Lys Lys Leu  
1 5

<210> 121  
<211> 7  
<212> PRT  
<213> Homo sapiens

<400> 121  
Gly Gly Lys Ala His Lys Leu  
1 5

<210> 122  
<211> 7  
<212> PRT  
<213> Homo sapiens

<220>  
<221> VARIANT  
<222> 6  
<223> Xaa = dR which is an isomer of Arg

<400> 122  
Gly Gly Lys Ala Arg Xaa Leu  
1 5

<210> 123  
<211> 7  
<212> PRT

23

<213> Homo sapiens

<220>

<221> VARIANT

<222> 5, 6

<223> Xaa = dR which is an isomer of Arg

<400> 123

Gly Gly Lys Ala Xaa Xaa Leu

1

5

<210> 124

<211> 5

<212> PRT

<213> Homo sapiens

<400> 124

Ala Gln Lys Arg Arg

1

5

<210> 125

<211> 5

<212> PRT

<213> Homo sapiens

<400> 125

Gly Lys Ser Arg Arg

1

5

<210> 126

<211> 5

<212> PRT

<213> Homo sapiens

<400> 126

Glu Gln Lys Arg Arg

1

5

<210> 127

<211> 5

<212> PRT

<213> Homo sapiens

<400> 127

Glu Ala Lys Arg Arg

1

5

<210> 128

<211> 5

<212> PRT

<213> Homo sapiens

<400> 128

Gly Gln Lys Arg Arg

1

5

<210> 129

24

```

<211> 5
<212> PRT
<213> Homo sapiens

<400> 129
Gly Ala Lys Arg Arg
1 5

<210> 130
<211> 5
<212> PRT
<213> Homo sapiens

<400> 130
Gly Lys Lys Arg Arg
1 5

<210> 131
<211> 5
<212> PRT
<213> Homo sapiens

<400> 131
Gly His Lys Arg Arg
1 5

<210> 132
<211> 5
<212> PRT
<213> Homo sapiens

<400> 132
Gly Lys Ala Phe Arg
1 5

<210> 133
<211> 5
<212> PRT
<213> Homo sapiens

<400> 133
Glu Lys Ala Gln Arg
1 5

<210> 134
<211> 5
<212> PRT
<213> Homo sapiens

<400> 134
Glu Lys Ala Arg Arg
1 5

<210> 135
<211> 7
<212> PRT
<213> Homo sapiens

```



25

<400> 135

Gly Gly Lys Ala Arg Arg Leu

1

5